REMARKS/ARGUMENTS

Submitted with the present Amendment is a Request for Continued Examination (RCE) under 37 CFR § 1.114 for the above-identified application. The Director is hereby authorized to charge the requisite RCE fee under 37 CFR § 1.17(e), any underpayment of fees, or credit any overpayments, to Deposit Account No. 20350.

By the present Amendment, claims 50, 57 and 61-63 are pending in this application. The invention, as defined by these claims, is directed to a method of designing a lead candidate (small molecule) having biophysical or biochemical activity against a biological target molecule (protein).

Claim Rejections - 35 U.S.C. §103

The Action has maintained the rejection of claims 50, 57 and 61-63 under 35 U.S.C. §103(a) as allegedly being *prima facie* obvious over the teachings of Dauter *et al., Acta Crystallographica D57:239-249 (2001),* in view of Congreve *et al., Agnew Chem. In. Ed. 42:4479-4482 (2003),* and/or Appleby *et al., Structure 7(6):629-641 (1999).* Applicants respectfully disagree.

Applicants respectfully disagree with the Action's assertion that our priority claim to U.S. provisional application serial no. 60/462,638 is improper. Our priority claim to the '638 provisional application may be found on page 3 of the attached Application Data Sheet as filed with the present application on April 9, 2004. This Sheet is in compliance with 37 CFR §1.76 (5) Domestic priority information, which constitutes the specific reference required by 35 U.S.C. §119(e). As previously described in our last response, pending claims 50, 57 and 61-63 are fully supported by the specification and claims in the '638 provisional application. Applicants respectfully request reconsideration and removal of this rejection over Congreve.

In the interest of moving prosecution along to the allowance of the pending claims, applicants point out that the invention, as defined by the claims, distinguishes over Dauter in view of Congreve and/or Appleby, by claiming a method of designing a lead candidate

(small molecule) having biophysical or biochemical activity against a biological target molecule (protein), by a) combining a crystalline biological target molecule (protein) with a mixture comprising at least two compounds (small molecules), wherein at least one of the compounds (small molecules) comprises a substituent having anomalous dispersion properties; b) determining the structure of at least one of the compounds (small molecules) in association with the biological target molecule (protein) using x-ray crystallographic analysis; and c) selecting information from the structure (small molecule and protein) to design the lead candidate (small molecule). As discussed below, none of these publications teaches or suggests any methods for designing a lead candidate (small molecule) having biophysical or biochemical activity against a biological target molecule (protein) as required by the instant claims.

Dauter does not teach or suggest any methods for designing a lead candidate (small molecule) as required by the instant claims. Instead, this publication teaches methods to determine a previously known macromolecular (protein) structure by soaking crystals of the macromolecule (protein) in salt solutions such as sodium bromide solutions. This publication does not teach or suggest any methods for designing a lead candidate (small molecule) by combining a crystalline biological target molecule (protein) with a mixture comprising at least two compounds (small molecules), wherein at least one of the compounds comprises a substituent having anomalous dispersion properties as required by the instant claims.

Congreve does not cure the defects of Dauter because this publication does not teach or suggest any methods for designing a lead candidate (small molecule) as required by the instant claims. Instead, this publication teaches dynamic combinatorial X-ray crystallography (DCX) for synthesizing and identifying inhibitors of the cyclin-dependent kinase 2 protein. This publication does not teach or suggest any methods for designing a lead candidate (small molecule) by combining a crystalline biological target molecule (protein) with a mixture comprising at least two compounds (small molecules), wherein at least one of the compounds comprises a substituent having anomalous dispersion properties as required by the instant claims.

Nor does Appleby cure the defects of Dauter and Congreve because this publication does not teach or suggest any methods for designing a lead candidate (small molecule) as required by the instant claims. Instead, this publication teaches methods to

determine the crystal structure of the biological target molecule (protein), namely 5'-deoxy-5'-methylthioadenosine phosphorylase (MTAP), bound to adenine alone and complexed with 5'-deoxy-5'-methylthioadenosine (MTA) and sulfate, using multiwavelength anomalous diffraction techniques wherein selenium is incorporated into the biological target molecule (protein), i.e., MTAP. This publication does not teach or suggest any methods for designing a lead candidate (small molecule) by combining a crystalline biological target molecule (protein) with a mixture comprising at least two compounds (small molecules), wherein at least one of the compounds comprises a substituent having anomalous dispersion properties as required by the instant claims.

Based on the teachings of Dauter, Congreve and Appleby, applicants respectfully submit that a *prima facie* case of obviousness has not been established for the claimed invention. Applicants respectfully request reconsideration and removal of these rejections.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6155.

Respectfully submitted,

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Application Data Sheet

Application Information

Application number::	
Filing Date::	
Application Type::	Regular
Subject Matter::	Utility
Suggested classification::	
Suggested Group Art Unit::	
CD-ROM or CD-R??::	
Number of CD disks::	
Number of copies of CDs::	
Sequence Submission::	
Computer Readable Form (CRF)?::	
Number of copies of CRF::	
Title::	COMPOUND LIBRARIES AND METHODS FOR DRUG DISCOVERY
Attorney Docket Number::	022132-001110US
Request for Early Publication::	No
Request for Non-Publication::	No
Suggested Drawing Figure::	8
Total Drawing Sheets::	8
Small Entity?::	Yes
Latin name::	
Variety denomination name::	
Petition included?::	No
Petition Type::	
Licensed US Govt. Agency::	
Contract or Grant Numbers One::	
Secrecy Order in Parent Appl.::	No

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Correspondence Information

Correspondence Customer Number:: 20350

Representative Information

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Domestic Priority Information

Application::	Continuity Type::	Parent Application::	Parent Filing Date::
This Application		60/462,638	04/11/03
This Application		60/531,197	12/19/03

Foreign Priority Information

Country:: Application number:: Filing Date::

Assignee Information

Assignee Name::
Street of mailing address::
City of mailing address::
State or Province of mailing address::
Country of mailing address::
Postal or Zip Code of mailing address::